

## REMARKS

Claims 1-24, 31-49, 51-56, and 58 have been canceled without prejudice or disclaimer. Claims 59-66 have been added. Claims 59-66 are supported by the specification and claims as originally filed.

Claims 59-66 are supported by the original specification (referring to the pages of the International Publication WO 01/66712) at, among other places, page 4, lines 9-14 (referring to the "modification" of an alpha-amylase in which a position "suitable for modification" is "identified"), page 13, lines 6-19 (in the context of discussion the derivation of the alpha-amylases, disclosing that the modification means the alteration of "naturally occurring amino acid residues," in other words, producing non-naturally occurring polypeptide sequences), page 24, lines 23-30 (again disclosing that the parent alpha-amylases are modified, and a modification is changing the naturally-occurring amino acid residue in the parent alpha-amylase).

The Examiner previously rejected the claims for use of the term "non-naturally occurring" as not supported by the specification. This term, however, is clearly supported, as illustrated in the above passages of the specification which state that the variants involve replacing a naturally occurring amino acid.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

### **I. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(b)**

Claims 25, 27-28 and 30 are rejected under 35 U.S.C. 102(b) as being anticipated by Outtrup et al. In summary, the Examiner alleges that although Outtrup et al. does not teach a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering), that the wild-type alpha-amylase of Outtrup et al. nevertheless reads on the claims because it has a lysine at one of the recited positions. The Examiner concludes that the claims therefore encompass the alpha-amylase of Outtrup et al. and therefore Outtrup et al. anticipates the claims. This rejection is respectfully traversed.

The alpha-amylase of Outtrup et al. does not read on the claims as the claims are directed to "variant" alpha-amylases having a "substitution" at an amino acid position 118, 320 and/or 458 (using SEQ ID NO:12 for numbering). As previously presented, the use of the term "variant" and "substitution" distinguishes the claimed alpha-amylases from the wild-type enzyme of Outtrup et al. which is neither a "variant" nor does it have a "substitution" at the recited position. It also clearly

does not have a substitution of "R118K", "R320K" or "R458K."

In response, in the Advisory Action, the Examiner alleges that the term "variant" can include variants made in nature, and moreover that the specification does not clearly limit variant to man made polypeptides. The Examiner further alleges that even accepting Applicants argument that variant means "man made," the claims are then "product-by-process" claims in which patentability is based on the product itself and the patentability of the product does not depend on the method steps.

Applicants respectfully traverse this rejection. Applicants respectfully submit that the specification clearly uses the term "variant" to refer to "man made" variants and not variants made in nature. Thus, even if a "variant" can be a natural variant, the specification defines variant as "man made." This is illustrated, e.g., in the specification at page 4, lines 9-14, page 13, lines 6-19, and page 24, lines 11-15, which clearly illustrate that the term variant means non-naturally occurring. In particular, the specification discloses that the variants have changes to the naturally-occurring amino acid, and therefore, are not found in nature.

In addition to the term variant, the claims also employ the term "substitution," which clearly makes the claimed variants "man made." In particular, the term "substitution" is identified in the specification as the result of identifying a suitable position and changing the "naturally-occurring" amino acid to a non-naturally occurring amino acid. See *id.*

Moreover, even assuming for the sake of argument that a variants can include natural variants, and the term "substitution" does not further clarify that the claims are directed to "man made" (i.e., non-natural) variants, Applicants have presented new claims 59-66. The claims are directed to a "non-naturally occurring, modified parent alpha-amylase" and further states that the "modification is a substitution of a K for the amino acid naturally occurring at said position in the parent alpha-amylase such that a K is not naturally present in said alpha-amylase prior to said modification." Clearly, natural variants are not encompassed by claims 59-66 which directed to alpha-amylase which are non-naturally occurring or modified and in which the modification is not naturally present in the parent alpha-amylase.

Accordingly, the claims are not anticipated by Outtrup et al because the claims do not encompass wild-type enzymes. Moreover, a skilled artisan would understand that the claims encompass non-naturally occurring alpha-amylases and do not encompass the naturally occurring alpha-amylase of Outtrup et al.

The Examiner further alleges that even accepting Applicants argument that variant means "man made," the claims are then "product-by-process" claims in which patentability is based on the

product itself and the patentability of the product does not depend on the method steps. The Board of Patent Appeals and Interferences has previously addressed the application of the principles of "product-by-process" claims to whether a natural polypeptide anticipates a recombination polypeptide. See *Ex Parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) (copy of decision attached). In *Ex Parte Gray*, the Board held that, although claimed as a product, the principles of "product-by-process" claims apply to the claimed Human nerve growth factor amino acid sequence, and that it is the burden of the Applicant to provide that the claimed recombinant product differs from the naturally isolated Human nerve growth factor.

The present application is distinguishable from the decision in *Ex Parte Gray* in that in this case, the claim language of the claimed product definitively excludes the prior art. In particular, claims 25-30, 50, 57 and 59-66 each contain claim language recitations which clearly avoid the prior art naturally occurring alpha-amylase. In particular, the prior art does not disclose "variant" alpha-amylases having "substitutions" (claims 25-20 and 50) or "non-naturally occurring" or "modified" alpha-amylases in which the modification is "not naturally present in the parent alpha-amylase" (claims 59-66). Thus, the issue of whether the claimed product is the same as the prior art is not at issue because the claim language distinguishes the prior art.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

## **II. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(e)**

Claims 25, 27-28 and 39 are rejected under 35 U.S.C. 102(e) as anticipated by US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031, and 6,887,986. The Examiner also alleges that although these patents do not teach a substitution of a lysine at an amino acid position selected from the group consisting of 118, 320 and 458 (using SEQ ID NO:12 for numbering), that the wild-type alpha-amylases disclosed nevertheless read on the claims. This rejection is respectfully traversed.

For the same reasons discussed above, the alpha-amylases of US Patent Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031 and 6,887,986 also do not read on the claims as they do not disclose variant alpha-amylases having a substitution of a lysine at a position selected from the group consisting of 118, 320 and 458 (claims 25-20 and 50) or the non-naturally occurring, modified parent alpha amylases (claims 59-66).

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

### **III. Double Patenting**

Claims 25, 27-28 and 30 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over US Patent Nos. 6,093,526, 6,187,576, 6,197,565, 6,204,232, 6,297,038 and 6,673,589. This rejection is respectfully traversed.

The Examiner alleges that the claims are not patentably distinct from the claims of the instant application because all of the patents claim "a sequence that is 90% identical to SEQ ID NO:12 and comprise a change at position 320 and 458." As previously discussed, it is respectfully submitted that the referenced patents do not disclose variant alpha-amylases having a substitution of a lysine at a position selected from the group consisting of 118, 320 and 458 of claims 25-20 and 50, or the non-naturally occurring, modified parent alpha amylases of claims 59-66. A non-naturally occurring alpha-amylase is not obvious from a naturally occurring alpha-amylase, and vice versa.

For the foregoing reasons, Applicants submit that the claims overcome the obviousness type double patenting rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

### **IV. Conclusion**

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

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